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Smoking and Other Risk Factors for Lung Cancer in Xuanwei, China

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In Xuanwei County, Yunnan Province, lung cancer mortality rates are among the highest in China in both males and females. Previous studies have shown a strong association of lung cancer mortality with indoor air pollution from 'smoky' coal combustion. In the present case-control study, 110 newly-diagnosed lung cancer patients and 426 controls were matched with respect to age, sex, occupation (all subjects were farmers), and village of residence (which provided matching with respect to fuel use). This design allowed assessment of known and suspected lung cancer risk factors other than those mentioned above. Data from males and females were analysed by conditional logistic regression. In females who do not smoke, the presence of lung cancer was statistically significantly associated with chronic bronchitis (odds ratio [OR] = 7.37, 95% confidence interval [CI]: 2.40–22.66) and family history of lung cancer (OR 4.18, 95% CI: 1.61–10.85). Females' results also suggested an association of lung cancer with duration of cooking food (OR 1.00, 9.18 and 14.70), but not with passive smoking (OR 0.77, 95% CI: 0.30–1.96). In males, lung cancer was significantly associated with chronic bronchitis (OR 7.32, 95% CI: 2.66–20.18), family history of lung cancer (OR 3.79, 95% CI: 1.70–8.42), and personal history of cooking food (OR 3.36, 95% CI: 1.27–8.88). In males a dose-response relationship of lung cancer with smoking index (years of smoking*amount of smoking) was shown by risks of 1.00, 2.61, 2.17 and 4.70.

Examination of Chinese nationwide cancer mortality statistics reveals that lung cancer mortality rates in Xuanwei County, Yunnan Province, are among the highest in China.[1] From 1973 through 1975, annualized male lung cancer death rates, age-adjusted to the 1964 China population, were 27.7 and 6.8 per 100 000 in Xuanwei and China, respectively. Corresponding mortalities in females were 25.3 and 3.2 per 100 000. Marked geographical variation in lung cancer mortality exists within Xuanwei. The county can be divided into high-, medium- and low-mortality areas, in which age-adjusted lung cancer mortalities in both sexes are 126.1, 20.9 and 6.0 per 100 000, respectively.

Xuanwei residents have traditionally burned three types of fuel, 'smoky' coal, 'smokeless' coal, and wood, for residential heating and cooking. Until the 1980s fuel was nearly always burned in an open, unventilated fire pit in the floor of the dwelling's main room; such fire pits are still widely used, though the use of ventilated stoves is increasing. Women have generally been responsible for starting and tending the domestic fire and cooking food, though men assume these responsibilities in some families.

Tobacco smoking is very rare in Xuanwei women, yet women's lung cancer rates are comparable to men's. Also, a survey of past fuel use showed that in the high-, medium- and low-mortality areas of Xuanwei, the percentages of families using smoky coal before 1958 were 87.6%, 60.1% and 6.1% respectively. Corresponding percentages of families using wood were 1.4%, 19.9% and 67.1%. Indoor concentrations of benzo(a)pyrene (BAP) averaged 627 ug/100 metres^3 (m^3) in the high-mortality area, and 46 ug/100 m^3 in the low-mortality area. In addition indoor pollution samples from the high-mortality area exhibited higher Ames-test mutagenicity than those from the low-mortality area.[2,3] All of these observations have served to suggest an association between indoor smoky coal burning and lung cancer in Xuanwei.

The case-control study reported here was designed to supplement existing information by assessing the influence of factors other than fuel type on the occurrence of lung cancer in Xuanwei. Such factors, includ-

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ing tobacco smoking, family history of lung cancer, history of chronic bronchitis, and cooking habits, have been associated with lung cancer in areas other than Xuanwei, but their importance as contributors to lung cancer in Xuanwei has not yet been systematically determined. The present study also allowed comparison of the relative impact of these factors in males and females.

MATERIALS AND METHODS

In Xuanwei, 93.4% of the total population were farmers in 1982. Because of this, and because lung cancer mortality in Xuanwei farmers is high,[2] this study was confined to farmers. Concentrating the target population tended to increase the validity of the findings.[4] Between November 1985 and December 1986, we identified 112 cases of newly-diagnosed lung cancer at Xuanwei hospitals and clinics. After exclusion of two patients with unknown addresses, 110 lung cancer patients (56 males and 54 females) were included in data analysis. Of these, 19 (17%) had been diagnosed on the basis of cytological/pathological findings, and the remainder on the basis of clinical histories and X-rays.

Controls were selected to match lung cancer patients with respect to age (±2 years), sex, and village of residence. Because fuel use habits and dwelling types are similar within individual Xuanwei villages, this design was expected to provide effective matching with respect to indoor fuel type and dwelling type.

Such matching was sought because it would increase the effectiveness with which factors other than fuel type could be assessed. Cases and controls were matched on village, with as many eligible controls included as possible. Therefore, we selected more controls for each case in a large village than in a small village. The numbers of controls per case varied from one to five. After exclusion of 26 controls because of erroneous questionnaire responses, 426 controls were included in data analysis, an average of 3.87 controls per case. There were 9 cases with 1 control, 15 cases with 2 controls, 15 with 3 controls, 13 with 4 controls, and 58 with 5 controls.

A standardized questionnaire of the closed-question type was developed. Study factors included tobacco use history, family and personal medical history, domestic fuel use history, indoor fuel use history, personal history of cooking food, dwelling type, ethnic group (nationality), and socioeconomic and educational levels. After strict interviewer training and field testing, this questionnaire was administered directly to all lung cancer patients and controls. No interviewer or study subject knew the purpose of the study and hypotheses.

A summary index of tobacco smoking was developed for each subject. The smoking index was calculated by multiplying the duration of smoking (in years) by the amount of tobacco smoked (in kilograms per month). A subject was considered to have a positive family history of lung cancer if at least one relative was reported to have had the disease. The relatives included subjects' parents, siblings and children, and parents' siblings. A subject was considered to have a positive history of chronic bronchitis if he or she had been diagnosed by a doctor to have this condition, or reported cough for at least three months per year for at least two years before the year of interview. A female subject was considered to have been exposed to passive smoking if there was at least one smoker (mainly husband) who lived in the same household.

To assess the effects of individual independent variables, unmatched, unadjusted odds ratios (ORs) were calculated.[5] Confidence intervals were calculated using Miettinen's method.[6] Dose-response relationships were examined for variables related to smoking and cooking. Trends within these relationships were tested by extension of the Mantel-Haenszel procedure.[7]

To develop adjusted estimates of ORs associated with selected factors and interactions, conditional logistic regression models were also constructed for males and females.[8] In these models, all variables were dichotomous, assuming values of 0 or 1. The selected risk factors and interactions were treated as independent variables, and the presence or absence of lung cancer was treated as the dependent variable. These analyses were performed using the PECAN program.[9,10]

RESULTS

Distributions of characteristics in cases and controls are presented by gender in Table 1. Age, family size, ethnic group, birthplace, educational level, and dwelling type were comparable in cases and controls, so these factors were not considered further in data analysis. The effect of active tobacco smoking was not evaluated in females, since only one female (a control subject) had ever smoked tobacco. The village matching provided effective matching on fuel type because fuel-use habits (type and average amount) were similar in cases and controls.

Crude and adjusted ORs for smoking and cooking habits are presented with 95% confidence intervals for males in Table 2. No relationship between lung cancer and ever having smoked was observed. There was a suggestion of monotonic dose-response relationships of lung cancer with the age at which smoking began, duration of smoking and amount smoked by month.

TABLE 1 *Comparison of lung cancer cases and controls, Xuanwei, China, 1985–1986*

Factor	Males		Females	
	Cases	Controls	Cases	Controls
Average age (years)	52	50	52	52
No. of people in family now	5.6	5.4	5.6	5.4
No. of people in family 20 years ago	5.8	5.5	5.9	5.5
Han nationality (%)	94.6	96.9	98.2	97.0
Born in Xuanwei (%)	100	100	100	98.0
Two-storey dwelling (%)	98.2	99.1	100	100
Amount of 'smoky' coal burnt (tons/year)	4.2	4.2	4.0	4.1
Amount of wood burnt (tons/year)	0.8	0.9	0.8	1.0

TABLE 2 *Odds ratios (OR) and 95% confidence intervals (CI) for lung cancer in males according to smoking and cooking, Xuanwei, China, 1985–1986*

Factor	Cases	Controls	ORc*	ORa**	95% CI
Ever-smoker					
No	4	19	1.00	1.00	
Yes	52	205	1.20	1.26	0.30– 5.26
Age of starting to smoke (years)					
Never	4	19	1.00	1.00	
>20	20	80	1.19	1.10	0.25– 4.93
≤20	32	125	1.22	1.39	0.32– 6.06
Trend (p value)			(p>0.05)		
Years of smoking					
0	4	19	1.00	1.00	
<35	30	146	0.98	1.07	0.25– 4.59
≥35	22	59	1.77	1.71	0.36– 8.12
Trend (p value)			(p>0.05)		
Amount of smoking (kg/per month)					
Never	4	19	1.00	1.00	
≤0.5	25	93	1.28	1.41	0.33– 6.09
0.6–1.0	20	93	1.02	1.09	0.24– 4.82
>1.0	7	19	1.75	1.91	0.32–11.40
Trend (p value)			(p>0.05)		
Smoking index†					
<2	4	30	1.00	1.00	
2–	24	99	1.82	2.61	0.69– 9.82
20–	16	74	1.62	2.17	0.55– 8.64
35–	12	21	4.28	4.70	1.03–21.40
Trend (p value)			(p<0.05)		
Often cooks food					
No	44	200	1.00	1.00	
Yes	12	24	2.27	3.36	1.27– 8.88

*ORc = Crude odds ratio.
**ORa = Odds ratio after adjustment by conditional logistic regression for other risk factors.
†Smoking index = Years of Smoking*Amount of smoking.

However, none of these relationships was statistically significant. In contrast, a statistically significant dose-response relationship of lung cancer with smoking index was observed. The adjusted OR in men who often cooked food (at least once a day) was 3.36 (95% CI: 1.27–8.88). The adjusted ORs were slightly larger than the crude ORs.

Crude and adjusted ORs for cooking and passive smoking are presented for females in Table 3. No dose-response relationship of lung cancer with age at which the woman began to cook food was observed, but the OR associated with the age at which the woman began to cook food (11–15 years old) was significant. Adjusted ORs associated with the duration of cooking were much larger than crude ORs. There was a suggestion of dose-response relationship of lung cancer with the duration of cooking food for the adjusted ORs. No relationship of lung cancer with passive smoking was observed.

Odds ratios for family history of lung cancer and personal history of chronic bronchitis were significantly associated with lung cancer in both sexes but duration of using an unventilated fire pit was not (Table 4). All conditional logistic regression ORs were larger than crude ORs in Table 4.

DISCUSSION

This study was intended to supplement previous studies which had shown a strong association of indoor smoky coal combustion with lung cancer in Xuanwei County.[2,3] Full understanding of lung cancer aetiology in Xuanwei, and comprehensive risk assessment of the effect of smoky coal use, require systematic assessment

TABLE 3 *Odds Ratios (OR) and 95% confidence intervals (CI) for lung cancer in females according to cooking and passive smoking, Xuanwei, China, 1985–1986*

Factor	Cases	Controls	ORc*	ORa**	95% CI
Age of starting to cook					
>15	13	73	1.00	1.00	
11–15	30	69	2.44	2.37	1.09– 5.15
≤10	11	60	1.03	1.25	0.45– 3.49
Trend (p value)			(p>0.05)		
Years of cooking					
≤30	7	53	1.00	1.00	
31–44	28	85	2.49	5.18	1.76– 47.49
≥45	19	64	2.25	14.70	1.61–134.03
Trend (p value)			(p>0.05)		
Passive smoking					
No	9	26	1.00	1.00	
Yes	45	176	0.74	0.77	0.30– 1.96

* ORc = Crude odds ratio.
** ORa = Odds ratio after adjustment by conditional logistic regression for other risk factors.

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TABLE 4 *Adjusted odds ratios (OR) and 95% confidence intervals (CI) for lung cancer in males and females, according to familial history of lung cancer, history of chronic bronchitis and years using unventilated fire pit, Xuanwei, China, 1985–1986*

Factor	Males			Females			Total		
	Case	Control	ORa* (95% CI)	Case	Control	ORa (95% CI)	Case	Control	ORa (95% CI)
Familial history of lung cancer									
No	41	200		45	192		86	392	
Yes	15	24	3.79 (1.70–8.42)	9	10	4.18 (1.61–10.85)	24	34	3.75 (2.05–6.83)
History of chronic bronchitis									
No	39	209		38	184		77	393	
Yes	17	15	7.32 (2.66–20.18)	16	18	7.37 (2.40–22.66)	33	33	7.61 (3.62–16.00)
Years using unventilated fire pit									
<45	22	107		21	84		43	191	
≥45	34	117	1.78 (0.46–6.93)	33	118	0.73 (0.20–2.60)	67	235	1.12 (0.46–2.74)

*ORa = Odds ratio after adjustment by conditional logistic regression for other risk factors.

not only of fuel use, but of other known and suspected risk factors as well. To achieve such an assessment, we chose a study design which provided effective case-control matching with respect to fuel type and average amount used as well as to age and gender.

Xuanwei is a very rural area. In the present study, almost all lung cancer patients were diagnosed by the county hospitals. Only 17% of the lung cancer cases were based on cytological/pathological findings, 83% were based on clinical histories and X-ray findings. Therefore, misclassification of the cases may exist in the study. However, other reasons may improve validity of lung cancer diagnosis in the study. Because of poor medical care in Xuanwei, most lung cancer patients had reached an advanced stage of the disease when diagnosed, and local doctors had wide experience of this diagnosis because of the high lung cancer morbidity in Xuanwei. In order to assess validity of the diagnosis, we also followed up a number of lung cancer patients from the study, almost all of whom died within six months of diagnosis.

In both males and females, the current study disclosed consistent and statistically significant associations of lung cancer with chronic bronchitis and positive family history of lung cancer. Lung cancer was also associated with the frequency of cooking food (in males) and the duration of cooking food (in females), even after the matching on fuel type inherent in the study design. Not surprisingly, lung cancer was associated with active smoking in males. No association with passive smoking was observed in females.

In Xuanwei, women are generally responsible for cooking food, so the variable 'cooks or does not cook food' could not be assessed in females. However, the ORs associated with the variable 'years of cooking' suggested that lung cancer risk increased with increase in duration of cooking (Table 3). There was no dose-response relationship between lung cancer and age at which a woman began to cook food. This observation may be due to the possibility that women who reported cooking food at less than ten years old did not really cook food at that age. The OR in males who often cooked food was over three times greater than in those who did not. It is likely that those who cook food inhale more coal-smoke pollution than those who do not. Wu *et al* reported that subjects exposed to burning coal used for heating or cooking in a stove or fireplace during the majority of childhood and the teenage years had a lung cancer risk 2.3 times higher than subjects who were not so exposed.[11] Wang *et al* have reported similar results from China.[12] Gao *et al* reported increased risk of lung cancer in Shanghai women who cook frequently with rapeseed oil.[13] This observation raises the question of whether pollutants associated not only with the cooking fuel but also with the cooking method promote lung cancer.

The observed association of lung cancer with positive family history of the illness may be attributable in part to recall bias. However, our results are consistent with other studies[14–17] which tends to reinforce the validity of the association. Our relative risk estimates for positive family history of lung cancer, 3.79 in males and 4.18 in females, were also similar to previous studies. The association may be due partly to the fact that a subject's relatives lived in the same environment as the subject for some time. Mulvihill has postulated that some abnormal types of gene might increase sensitivity to environmental carcinogens.[18] Further research will be necessary to elucidate and distinguish the roles of genetic and environmental factors in carcinogenesis.

Tobacco smoking is generally accepted to be a major cause of lung cancer.[19–22] We observed an association of lung cancer with tobacco smoking in males, and this observation tended to enhance confidence in the results. However, the association was weaker than has been reported in many previous studies.[13,19] When considered individually, duration of smoking, amount of smoking, and age at which smoking began were only weakly associated with the illness. Only the smoking index derived by multiplying duration by amount of smoking was significantly associated with lung cancer.

These observations may be due partly to the fact that only 23 (8.2%) of 280 males in this study were lifetime non-smokers. In such a small comparison group, even fairly small changes in the distribution of non-smokers between cases and controls could have produced marked differences in observed ORs associated with smoking. More importantly many farmers in Xuanwei smoke tobacco through a long bamboo cylinder partly filled with water and the passage of smoke through the water may filter out carcinogenic substances. Studies comparing the composition of water-filtered to unfiltered tobacco smoke are currently in progress.

It is also quite conceivable that the large amount of air pollutants inhaled during indoor smoky coal burning in Xuanwei partly overwhelm the carcinogenic effect of tobacco smoking. For example, as mentioned above, the average indoor concentration of BAP in the Xuanwei region of high lung cancer mortality was 627 ug/100 m^3 in a recent survey. An individual inhaling 12 m^3 of air per day might therefore inhale 9154 ug of BAP in a year if he or she spent eight hours per day indoors. In contrast, an individual smoking 20 cigarettes per day might be expected to inhale only about 700 ug of BAP in one year.[23] Thus, it is not especially surprising that the ORs associated with smoking in Xuanwei males were smaller than reported in other studies. Because unusual environmental conditions prevail in Xuanwei, it would not be advisable to generalize these ORs to other areas.

Smoking is very rare in Xuanwei females. In addition, we observed no association of lung cancer with passive smoking in females. Such an association has been reported in several previous investigations.[24–27] In non-smoking women in Shanghai, Gao *et al* observed a limited association of lung cancer with passive smoking; in that study the relative risk ranged from 1.0 in women living less than 20 years with a smoking husband to 1.7 in those living with a smoking husband for at least 40 years.[13] However Koo *et al* have not observed a consistent association of lung cancer with passive smoking in Chinese women.[28–30] These authors also stated that correlates of passive smoking such as diet and socioeconomic status can act as important confounders when the health risks of passive smoking are evaluated.[31] The heavy indoor air pollution in Xuanwei may also overwhelm the carcinogenic effect of passive smoking. The effect of passive smoking on lung cancer may depend on local environmental factors and results obtained in a given region may therefore not be applicable to other regions.

In summary, this study was undertaken to supplement existing evidence showing a strong association of lung cancer with indoor use of smoky coal in Xuanwei. Our results disclose important associations of lung cancer with factors other than fuel type and therefore indicate that these factors must be considered in any comprehensive, quantitative risk assessment of lung cancer in Xuanwei. Our results also confirm indirectly that smoky coal pollution is an important determinant of lung cancer in Xuanwei. A separate case-control study, which will allow simultaneous direct analysis of the effects of indoor air pollution and other known and suspected lung cancer risk factors in Xuanwei, is currently in progress.

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